UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/847,935	05/03/2001	David F. Woodward	D2914	6555

33197 7590 05/08/2006

STOUT, UXA, BUYAN & MULLINS LLP
4 VENTURE, SUITE 300
IRVINE, CA 92618

EXAMINER	
FUBARA, BLESSING M	

ART UNIT	PAPER NUMBER
1618	

DATE MAILED: 05/08/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/847,935	WOODWARD ET AL.	
	Examiner	Art Unit	
	Blessing M. Fubara	1618	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *17 March 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *60-66,68,72,73,77 and 87-90* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *60-66,68,72,73,77 and 87-90* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Examiner acknowledges amendment and remarks filed 03/17/06. Claims 60-66, 68, 72, 73, 77 and 87-90 are pending. Receipt is also acknowledged for Notice of Appeal filed 1/20/06.

Applicants' argument with respect to DeSantis under 35 USC 102 (b) has been considered. The argument that prostaglandin is not a fatty acid is not persuasive because applicants' specification at page 13, second full paragraph identifies prostaglandin as a complex fatty acid. However, this Office action communication is made non-final because Examiner did not identify prostaglandin as an efficacy-enhancing component.

The Invention:

The rejections below are based on applicants' claim (claim 60) to composition comprising ion-pair complex comprising a therapeutic component that is adrenergic agonist, efficacy enhancing component and a carrier component, which includes saline. The efficacy enhancing component is selected form fatty acid, anionic polymers and mixtures thereof. The efficacy enhancing component "being effective to enhance the movement of the therapeutic component across a lipid membrane, or biological membrane under physiological conditions" is a property/function of the efficacy enhancing component and a property/function of a product/material or the efficacy enhancing agents is an inherent feature of the product/material or efficacy enhancing component. An ion-pair complex forms between pairs of ions having opposite charge. As is taught in applicants' specification at paragraph 77 of the published application, a complex forms when efficacy-enhancing component is added to a solution containing a therapeutic agent. Thus a solution containing therapeutic component and efficacy

enhancing component would have complex formed between the efficacy enhancing component and the therapeutic component.

In claim 87, the efficacy-enhancing component in is selected form fatty acid, anionic polymers and mixtures thereof. "Effective to enhance movement of the therapeutic component across a lipid membrane, or a biological membrane ...efficacy enhancing component" is a property of the composition. According to MPEP 2112.01 [R-3] II, *"products of identical chemical composition can not have mutually exclusive properties." A chemical composition and its properties are inseparable. Therefore, if the prior art teaches the identical chemical structure, the properties applicant discloses and/or claims are necessarily present. In re Spada, 911 F.2d 705, 709, 15 USPQ2d 1655, 1658 (Fed. Cir. 1990.).*

Claim Rejections - 35 USC § 102

1. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

2. Claims 87 and 88 are rejected under 35 U.S.C. 102(b) as being anticipated by DeSantis, Jr. et al. (US 5,811,443).

DeSantis discloses combination of at least one clonidine derivative, which is an alpha-2-adrenergic agonist, at least one prostaglandin (abstract; column 2, lines 25-37); the composition

may additionally contain anionic mucomimetic polymers in amounts of between about 0.05 and about 8.0 wt% and specifically pourable liquid formulations contain between about 0.05 and 2.0 wt % (column 8, lines 57-64) of the anionic polymers; the composition further comprises agents for adjusting tonicity and osmolality and those agents include sodium chloride, potassium chloride, mannitol, dextrose, glycerine and propylene glycol (column 8, lines 32-36) and the tonicity agents are used in amounts of between about 0.1 to about 10.0 wt% (column 8, lines 36-38). The composition is aqueous and has pH of between 3.5 and 8.0 and osmolality of between 280 to 320 milliOsmoles per kilogram (column 9, lines 35-37).

Prostaglandin is physiologically active compound derived from fatty acid. Prostaglandin is present at amounts of 0.00001 to 0.2 wt% (column 8, lines 7 and 8; claim 12); prostaglandin is a complex fatty acid as described in the as filed specification at page 13, second full paragraph. The anionic polymer and prostaglandin are efficacy-enhancing components. DeSantis discloses that the ratio of prostaglandin to clonidine is 1:1 to 1:10,000 (column 8, lines 14-17); and the ratio of 1:1 meets the limitation of claim 87. A solution of sodium chloride and water is saline and meets the limitation of saline in claim 1. Since according the applicants' specification, a complex forms between the therapeutic component and the efficacy-enhancing component in solution, it is plausible that a complex is formed between the clonidine, which is the therapeutic component and the anionic polymer, which is the efficacy-enhancing component.

The upper limit amount of the ionic polymer of about 2 wt% of the prior art lies within the efficacy enhancing polymer ranging in amounts of greater that 0.2% and less than 10%, the 2 wt% is less than 10%. Clonidine is alpha-2-adrenergic agonist meeting the limitation of claims

88. A pH of about 8 is greater that about 7 and lies between about 7 and about 9 and DeSantis. DeSantis is suitable for topical ophthalmic application (see claim 6).

Therefore, DeSantis meets the limitations of the designated claims.

3. The rejection of claims 60-63, 65, 66, 68, 72 and 73 under 35 U.S.C. 102(e) as being anticipated by Beck et al. (US 6,358,935) is withdrawn in view of the amendment to claim 60 that requires the claim to have fatty acid. Beck anticipates new claims 87, 89 and 90 according to the rejection below.

4. Claims 87, 88 and 90 are rejected under 35 U.S.C. 102(e) as being anticipated by Beck et al. (US 6,358,935).

Beck discloses composition comprising brimonidine (0.2% w/v), sodium carboxymethylcellulose (0.5%) and cyclodextrin (present in Example 2); the composition is at pH of 7.4 (Examples 1 and 2) and in saline (column 6, line 59). pH of 7.4 is greater than 7 and lies between the recited pH of 7-9 (claims 65 and 66). Specifically, Beck discloses the formation of complex between cyclodextrin and the therapeutic agent (column 6, lines 18-40). The carboxymethylcellulose meets the limitation of an additional efficacy-enhancing component of claim 77. The ratio of the therapeutic agent quinoxaline to the cellulose is 1:1 in example 1.

The applied reference has a common assignee with the instant application. Based upon the earlier effective U.S. filing date of the reference, it constitutes prior art under 35 U.S.C. 102(e). This rejection under 35 U.S.C. 102(e) might be overcome either by a showing under 37 CFR 1.132 that any invention disclosed but not claimed in the reference was derived from the

inventor of this application and is thus not the invention "by another," or by an appropriate showing under 37 CFR 1.131.

Claim Rejections - 35 USC § 103

5. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

6. Claims 60, 61, 64-66 and 68 are rejected under 35 U.S.C. 103(a) as being unpatentable over DeSantis, Jr. et al. (US 5,811,443).

DeSantis discloses combination of at least one clonidine derivative, which is an alpha-2-adrenergic agonist, at least one prostaglandin (abstract; column 2, lines 25-37); the composition may additionally contain anionic mucomimetic polymers in amounts of between about 0.05 and about 8.0 wt% and specifically pourable liquid formulations contain between about 0.05 and 2.0 wt % (column 8, lines 57-64) of the anionic polymers; the composition further comprises agents for adjusting tonicity and osmolality and those agents include sodium chloride, potassium chloride, mannitol, dextrose, glycerine and propylene glycol (column 8, lines 32-36) and the tonicity agents are used in amounts of between about 0.1 to about 10.0 wt% (column 8, lines 36-38). The composition is aqueous and has pH of between 3.5 and 8.0 and osmolality of between 280 to 320 milliOsmoles per kilogram (column 9, lines 35-37).

Prostaglandin is physiologically active compound derived from fatty acid and is listed in the instant specification as a complex fatty acid. The anionic polymer is the efficacy-enhancing

component. The comprising language of claim 60 is open and does not exclude the presence of the anionic polymer. A solution of sodium chloride and water is saline. Since according the applicants' specification, a complex forms between the therapeutic component and the efficacy-enhancing component in solution, it is plausible that a complex is formed between the clonidine, which is the therapeutic component and the prostaglandin or the anionic polymer, which is the efficacy-enhancing component.

Prostaglandin is present at amounts of 0.00001 to 0.2 wt% (column 8, lines 7 and 8; claim 12). The upper limit amount of the prostaglandin in DeSantis at 0.2 wt%, the efficacy enhancing component, is less than the lower limit of the fatty acid of greater than 0.2% of claim 60. However, greater than 0.2% is close to 0.2 % and there is no demonstration in applicants' specification that an efficacy enhancing component, and specifically fatty acid, in an amount of 0.2% would not be effective in the composition. Clonidine is alpha-2-adrenergic agonist. A pH of about 8 is greater that about 7 and lies between about 7 and about 9 and DeSantis thus meets the limitations of claims 65 and 66. While the recitation of "opthalmically acceptable" in claim 68 is a property of the formulation or the intended use of the formulation, it is noted that the composition of DeSantis is suitable for topical ophthalmic application (see claim 6 of DeSantis).

Regarding claim 64, DeSantis suggests that at least one clonidine derivative can be used in the composition, which implicates more than one clonidine use. It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to prepare the composition with more than one clonidine derivative in light of the suggestion by DeSantis. One having ordinary skill in the art would have been motivated to include at least two clonidine derivatives with the expectation of obtaining synergistic effect from the clonidine derivatives.

The efficacy enhancing component, in the case of DeSantis, prostaglandin, is capable of reducing intraocular pressure as disclosed by DeSantis. Therefore, the amount of prostaglandin is a result-effective variable, whose optimum workable range can be optimized.

Therefore, it would have been obvious to one of ordinary skill in the art at the time the invention was made to prepare the clonidine containing composition having 0.2% prostaglandin. One having ordinary skill in the art would have been motivated to optimize the amount of prostaglandin with the expectation that the optimized amount would be more effective in reducing intraocular pressure. Generally, differences in amounts of the disintegration agent will not support the patentability of the subject matter encompassed by the prior art unless there is evidence indicating such amount is critical. "W[here] the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation." In re Aller, 220 F.2d 454, 456, 105 USPQ 233, 235 (CCPA 1955).

7. Claims 60, 62, 63, 72, 73 and 77 are rejected under 35 U.S.C. 103(a) as being unpatentable over DeSantis, Jr. et al. (US 5,811,443) in view of Gluchowski (US 5,021,416).

DeSantis is described immediately above. The formulation of DeSantis is used to treat glaucoma or ocular hypertension. The formulation of DeSantis contains clonidine. The composition of DeSantis does not contain quinoxaline. However, Gluchowski discloses formulation containing quinoxaline, which when administered reduces or maintains intraocular pressure and the composition is used for the management of glaucoma (abstract; column 2, lines 44-53). Therefore, it would have been obvious to one of ordinary skill in the art at the time the invention was made to use the composition of DeSantis for the management of glaucoma or ocular hypertension. One having ordinary skill in the art would have been motivated to

substitute one therapeutic agent for another where both therapeutic agents are known in the art to treat glaucoma and to reduce or maintain ocular pressure. In this case, clonidine and quinoxaline are known to be used for management of ocular pressure and glaucoma. Therefore, quinoxaline, which is disclosed by Gluchowski to have effect on glaucoma and ocular pressure can be used in the composition of DeSantis in place of the clonidine with the expectation that the new composition would treat glaucoma and ocular pressure.

8. Claim 89 is rejected under 35 U.S.C. 103(a) as being unpatentable over Beck et al. (US 6,358,935).

Beck is described above. Beck does not disclose the quinoxaline of claim 89. One quinoxaline can be substituted for another and expect to obtain the same effect. Thus, it would have been obvious to one of ordinary skill in the art at the time the invention was made to use the teaching of Beck where the composition comprises methylcellulose and/or cyclodextrin and substitute 2-imidazolin-2-ylamino) quinoxaline for brimonidine tartrate with the expectation that the composition would produce the same effect in when administered to the eye.

9. The rejection of claims 60-63, 65, 66, 72, 73 and 77 under 35 U.S.C. 103(a) as being unpatentable over Gil et al. (US 6,294,553) is withdrawn in view of applicants' persuasive argument that Gil does not disclose any concentration of the efficacy enhancing components.

The prior art made of record and not relied upon is considered pertinent to applicant's disclosure. Uehara et al. In JP 11-130656 discloses a composition comprising fatty acid and alpha adrenergic inhibitor (English abstract). Clonidine, an alpha-2-adrenergic agonists is an alpha adrenergic inhibitor (see paragraph 43 of US 2005/0191245 as a teaching reference).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Blessing M. Fubara whose telephone number is (571) 272-0594. The examiner can normally be reached on 7 a.m. to 5:30 p.m. (Monday to Thursday).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael G. Hartley can be reached on (571) 272-0616. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Blessing Fubara
Patent Examiner
Tech. Center 1600